Letters to the Editor

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The ACCESS Study

To the Editor:

The report on the ACCESS study by Schrader et al stated that the clinical benefit in favor of the candesartan-treated group as compared with the control group was unrelated to blood pressure level, as both groups had similar blood pressure readings.1 This assertion may be incorrect as the reported blood pressure was derived from relatively infrequent readings taken by different nurses manually or with automated devices. This approach can be unreliable due to interobserver and interdevice variation and also the fact that the readings are not representative of the true 24-hour blood pressure load.2 A more valid assessment of overall blood pressure status can be obtained by noninvasive 24-hour ambulatory blood pressure monitoring.3 The authors stated that automatic 24-hour blood pressure recordings were actually obtained in all patients on day 7 of the study. The results of these data were not presented but would be very helpful, as they would enable a valid comparison of blood pressure between groups and allow correlation with clinical outcome.

Furthermore, the authors speculated that the better outcome of the treated group might be related to effects of candesartan on autonomic nervous system regulation. Evidence for this may also be seen from the 24-hour blood pressure profiles. It is known that in patients with autonomic nervous system dysfunction, the physiological day-night blood pressure difference is reduced or abolished (“nondipping”),4 and a similar derangement is also seen in their 24-hour heart rate profile.4 It has already been shown that, following a stroke, patients with nondipping have a worse outcome than patients with a normal diurnal blood pressure pattern.5 Thus, information from the authors about the 24-hour blood pressure and heart rate profiles may contribute to interpretation of the study findings.

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Response

The questions asked by Panayiotou and Fotherby have been discussed by the ACCESS authors as well. Of course, some additional information about the 24-hour blood pressure is very interesting, but it has to be considered that this is a subgroup analysis that has not been defined in the study protocol prospectively.

First of all, there was a high rate of patients with nondipping (<10% blood pressure decrease mean-night versus mean-daytime) in the ambulatory blood pressure monitoring (ABPM) on day 7 after stroke. There were also 4.8% of patients showing an inverse blood pressure rhythm. More than two thirds of the patients of each group were nondipped with a slightly greater number in the candesartan-treated group (72.3% versus 68.2%), but this difference was not significant.

Of all patients, 54.9% showed nondipping of the heart rate (<10% decrease of mean heart rate nighttime versus daytime) on day 7 (placebo group 53.5%, candesartan cilexetil group 56.3% [NS]); 59.3% of patients with nondipping in blood pressure showed nondipping in heart rate as well, and 45.6% with dipping in blood pressure showed nondipping in heart rate.

Concerning prognosis of the patients, there is an interesting correlation of admission blood pressure and nondipping in ABPM on day 7. There was a significantly higher rate of primary events among patients with nondipping at ABPM on day 7 if they had a systolic admission blood pressure ≥200 mm Hg compared with those with a systolic admission blood pressure <200 mm Hg (15.2% versus 4.4%, P = 0.013 [Fisher’s exact test]).

So we conclude that initial blood pressure values ≥200 mm Hg at hospitalization in combination with nondipping in the ABPM on day 7 are associated with a poorer prognosis on patient outcome. The percentage of these patients did not differ between the placebo and candesartan group. In a log linear model analysis with treatment (placebo/candesartan), systolic blood pressure on admission, and dipping in ABPM on day 7, all 3 factors have an independent and statistically significant influence on the end points. Overall candesartan cilexetil reduces the end points by about 50%. Systolic blood pressure at admission ≥200 mm Hg doubles the risk of end points. High blood pressure and blood pressure rhythm have not confounded the effect of the therapy.

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